

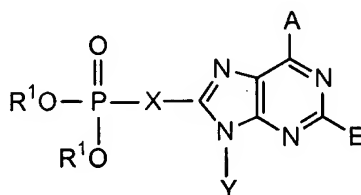
AMENDMENTS

In the Claims

Please amend the claims as indicated below. A complete set of all claims previously submitted, including the status for each claim, immediately follows below.

1. – 44. Cancelled

45. (New) A method of preventing diabetes in animals comprising administering to animals at risk of developing diabetes a pharmaceutically effective amount of a compound of formula 1:



wherein

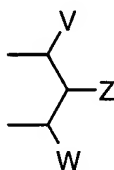
A is selected from the group consisting of $-\text{NR}^8$, $-\text{NHSO}_2\text{R}^3$, $-\text{OR}^5$, $-\text{SR}^5$, halo, lower alkyl, $-\text{CON}(\text{R}^4)_2$, guanidino, amidino, $-\text{H}$, and perhaloalkyl;

E is selected from the group consisting of $-\text{H}$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-\text{CN}$, and $-\text{NR}^7_2$;

X is selected from the group consisting of $-\text{alk-NR}-$, alkylene, alkenylene, alkynylene, arylene, heteroarylene, $-\text{alk-NR-alk}-$, $-\text{alk-O-alk}-$, $-\text{alk-S-alk}-$, $-\text{alk-S}-$, alicyclicene, heteroalicyclicene, 1,1-dihaloalkylene, $-\text{C}(\text{O})\text{-alk}-$, $-\text{NR-C}(\text{O})\text{-NR}'-$, $-\text{alk-NR-C}(\text{O})-$, $-\text{alk-C}(\text{O})\text{-NR}-$, $-\text{Ar-alk}-$, and $-\text{alk-Ar}-$, all optionally substituted, wherein each R and R' is independently selected from $-\text{H}$ and lower alkyl, and wherein each "alk" and "Ar" is an independently selected alkylene or arylene, respectively;

Y is selected from the group consisting of $-\text{H}$, alkyl, alkenyl, alkynyl, aryl, alicyclic, heteroalicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-\text{C}(\text{O})\text{R}^3$, $-\text{S}(\text{O})_2\text{R}^3$, $-\text{C}(\text{O})\text{-OR}^3$, $-\text{CONHR}^3$, $-\text{NR}^2_2$, and $-\text{OR}^3$, all except H are optionally substituted;

R^1 is independently selected from the group consisting of $-H$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$ -aryl, -alk-aryl, $-C(R^2)_2$ OC(O)NR²₂, $-NR^2$ $-C(O)-R^3$, $-C(R^2)_2$ $-OC(O)R^3$, $-C(R^2)_2$ $-O-C(O)OR^3$, $-C(R^2)_2$ OC(O)SR³, -alk-S- $C(O)R^3$, -alk-S-S-alkylhydroxy, and -alk-S-S-S-alkylhydroxy, or together R^1 and R^1 are -alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2$ OH, $-CH_2$ OCOR³, $-CH_2$ OC(O)SR³, $-CH_2$ OCO₂ R³, $-SR^3$, $-S(O)R^3$, $-CH_2$ N₃, $-CH_2$ NR²₂, $-CH_2$ Ar, $-CH(Ar)OH$, $-CH(CH=CR^2 R^2)OH$, $-CH(C \equiv CR^2)OH$, and $-R^2$;

with the provisos that:

- a) V, Z, W are not all $-H$; and

b) when Z is $-R^2$, then at least one of V and W is not $-H$ or $-R^9$;

R^2 is selected from the group consisting of R^3 and $-H$;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of $-H$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower alicyclic, and lower heteroalicyclic;

R^6 is independently selected from the group consisting of $-H$, and lower alkyl;

R^7 is independently selected from the group consisting of $-H$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

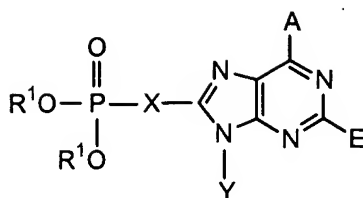
R^8 is independently selected from the group consisting of $-H$, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together said R^8 groups form a bidendate alkylene;

R^9 is selected from the group consisting of alkyl, aralkyl, alicyclic, and heteroalicyclic;

R^{10} is selected from the group consisting of $-H$, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-OH$, $-NH_2$ and $-OR^3$; and pharmaceutically acceptable prodrugs and salts thereof.

46. (New) A method of treating impaired glucose tolerance comprising administering to patients in need thereof a pharmaceutically effective amount of an FBPase inhibitor of formula 1:



wherein

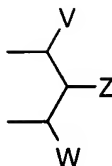
A is selected from the group consisting of $-\text{NR}^8$, $-\text{NHSO}_2 \text{R}^3$, $-\text{OR}^5$, $-\text{SR}^5$, halo, lower alkyl, $-\text{CON}(\text{R}^4)_2$, guanidino, amidino, $-\text{H}$, and perhaloalkyl;

E is selected from the group consisting of $-\text{H}$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-\text{CN}$, and $-\text{NR}^7_2$;

X is selected from the group consisting of $-\text{alk}-\text{NR}-$, alkylene, alkenylene, alkynylene, arylene, heteroarylene, $-\text{alk}-\text{NR}-\text{alk}-$, $-\text{alk}-\text{O}-\text{alk}-$, $-\text{alk}-\text{S}-\text{alk}-$, $-\text{alk}-\text{S}-$, alicyclicene, heteroalicyclicene, 1,1-dihaloalkylene, $-\text{C}(\text{O})-\text{alk}-$, $-\text{NR}-\text{C}(\text{O})-\text{NR}'-$, $-\text{alk}-\text{NR}-\text{C}(\text{O})-$, $-\text{alk}-\text{C}(\text{O})-\text{NR}-$, $-\text{Ar}-\text{alk}-$, and $-\text{alk}-\text{Ar}-$, all optionally substituted, wherein each R and R' is independently selected from $-\text{H}$ and lower alkyl, and wherein each "alk" and "Ar" is an independently selected alkylene or arylene, respectively;

Y is selected from the group consisting of $-\text{H}$, alkyl, alkenyl, alkynyl, aryl, alicyclic, heteroalicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-\text{C}(\text{O})\text{R}^3$, $-\text{S}(\text{O})_2 \text{R}^3$, $-\text{C}(\text{O})-\text{OR}^3$, $-\text{CONHR}^3$, $-\text{NR}^2_2$, and $-\text{OR}^3$, all except H are optionally substituted;

R^1 is independently selected from the group consisting of $-\text{H}$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-\text{C}(\text{R}^2)_2$ -aryl, $-\text{alk}-\text{aryl}$, $-\text{C}(\text{R}^2)_2 \text{OC}(\text{O})\text{NR}^2_2$, $-\text{NR}^2-\text{C}(\text{O})-\text{R}^3$, $-\text{C}(\text{R}^2)_2-\text{OC}(\text{O})\text{R}^3$, $-\text{C}(\text{R}^2)_2-\text{O}-\text{C}(\text{O})\text{OR}^3$, $-\text{C}(\text{R}^2)_2 \text{OC}(\text{O})\text{SR}^3$, $-\text{alk}-\text{S}-\text{C}(\text{O})\text{R}^3$, $-\text{alk}-\text{S}-\text{S}-\text{alkylhydroxy}$, and $-\text{alk}-\text{S}-\text{S}-\text{S}-\text{alkylhydroxy}$, or together R^1 and R^1 are $-\text{alk}-\text{S}-\text{S}-\text{alk}-$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxy carboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxy carboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-\text{CH}_2 \text{ OH}$, $-\text{CH}_2 \text{ OCOR}^3$, $-\text{CH}_2 \text{ OC(O)SR}^3$, $-\text{CH}_2 \text{ OCO}_2 \text{ R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2 \text{ N}_3$, $-\text{CH}_2 \text{ NR}^2_2$, $-\text{CH}_2 \text{ Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH}(\text{CH}=\text{CR}^2 \text{ R}^2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all $-\text{H}$; and
- b) when Z is $-\text{R}^2$, then at least one of V and W is not $-\text{H}$ or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and $-\text{H}$;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower alicyclic, and lower heteroalicyclic;

R^6 is independently selected from the group consisting of $-H$, and lower alkyl;

R^7 is independently selected from the group consisting of $-H$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

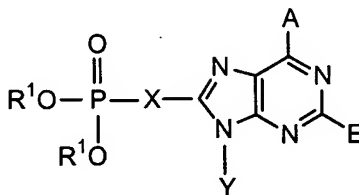
R^8 is independently selected from the group consisting of $-H$, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together said R^8 groups form a bidendate alkylene;

R^9 is selected from the group consisting of alkyl, aralkyl, alicyclic, and heteroalicyclic;

R^{10} is selected from the group consisting of $-H$, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-OH$, $-NH_2$ and $-OR^3$; and pharmaceutically acceptable prodrugs and salts thereof.

47. (New) A method of treating insulin resistance comprising administering to patients in need thereof a pharmaceutically effective amount of an FBPase inhibitor of formula 1:



wherein

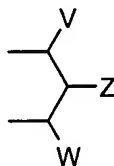
A is selected from the group consisting of $-NR^8$, $-NHSO_2 R^3$, $-OR^5$, $-SR^5$, halo, lower alkyl, $-\text{CON}(R^4)_2$, guanidino, amidino, $-H$, and perhaloalkyl;

E is selected from the group consisting of -H, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and -NR⁷₂;

X is selected from the group consisting of -alk-NR-, alkylene, alkenylene, alkynylene, arylene, heteroarylene, -alk-NR-alk-, -alk-O-alk-, -alk-S-alk-, -alk-S-, alicyclicene, heteroalicyclicene, 1,1-dihaloalkylene, -C(O)-alk-, -NR-C(O)-NR', -alk-NR-C(O)-, -alk-C(O)-NR-, -Ar-alk-, and -alk-Ar-, all optionally substituted, wherein each R and R' is independently selected from -H and lower alkyl, and wherein each "alk" and "Ar" is an independently selected alkylene or arylene, respectively;

Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, heteroalicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, -C(O)R³, -S(O)₂R³, -C(O)-OR³, -CONHR³, -NR²₂, and -OR³, all except H are optionally substituted;

R¹ is independently selected from the group consisting of -H, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, -C(R²)₂-aryl, -alk-aryl, -C(R²)₂OC(O)NR²₂, -NR²-C(O)-R³, -C(R²)₂-OC(O)R³, -C(R²)₂-O-C(O)OR³, -C(R²)₂OC(O)SR³, -alk-S-C(O)R³, -alk-S-S-alkylhydroxy, and -alk-S-S-S-alkylhydroxy, or together R¹ and R¹ are -alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R¹ and R¹ are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R⁹; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, carboxy,

or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-\text{CH}_2 \text{OH}$, $-\text{CH}_2 \text{OCOR}^3$, $-\text{CH}_2 \text{OC(O)SR}^3$, $-\text{CH}_2 \text{OCO}_2 \text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2 \text{N}_3$, $-\text{CH}_2 \text{NR}^2_2$, $-\text{CH}_2 \text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH}(\text{CH}=\text{CR}^2 \text{R}^2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all $-\text{H}$; and
- b) when Z is $-\text{R}^2$, then at least one of V and W is not $-\text{H}$ or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and $-\text{H}$;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower alicyclic, and lower heteroalicyclic;

R^6 is independently selected from the group consisting of $-\text{H}$, and lower alkyl;

R^7 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-\text{C(O)R}^{10}$;

R^8 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-\text{C(O)R}^{10}$, or together said R^8 groups form a bidendate alkylene;

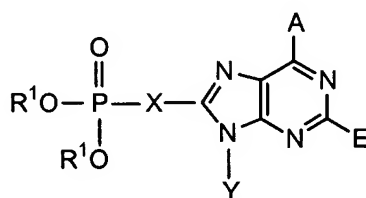
R^9 is selected from the group consisting of alkyl, aralkyl, alicyclic, and heteroalicyclic;

R^{10} is selected from the group consisting of $-H$, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-OH$, $-NH_2$ and $-OR^3$; and pharmaceutically acceptable prodrugs and salts thereof.

48. (New) The method of claim 1 wherein said animals at risk of developing diabetes have a disease or condition selected from the group consisting of impaired glucose tolerance, insulin resistance, hyperglycemia, obesity, accelerated gluconeogenesis, and increased hepatic glucose output.

49. (New) A method of treating or preventing a disease or condition selected from the group consisting of hyperlipidemia, atherosclerosis, ischemic injury, and hypercholesterolemia which comprises administering to an animal in need thereof a pharmaceutically effective amount of an FBPase inhibitor of formula 1:



wherein

A is selected from the group consisting of $-NR^8$, $-NHSO_2 R^3$, $-OR^5$, $-SR^5$, halo, lower alkyl, $-\text{CON}(R^4)_2$, guanidino, amidino, $-H$, and perhaloalkyl;

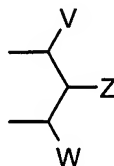
E is selected from the group consisting of $-H$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-\text{CN}$, and $-NR^7$; .

X is selected from the group consisting of $-\text{alk-NR}-$, alkylene, alkenylene, alkynylene, arylene, heteroarylene, $-\text{alk-NR-alk}-$, $-\text{alk-O-alk}-$, $-\text{alk-S-alk}-$, $-\text{alk-S}-$, alicyclicene,

heteroalicyclicene, 1,1-dihaloalkylene, $-C(O)-alk-$, $-NR-C(O)-NR'$, $-alk-NR-C(O)-$, $-alk-C(O)-NR-$, $-Ar-alk-$, and $-alk-Ar-$, all optionally substituted, wherein each R and R' is independently selected from $-H$ and lower alkyl, and wherein each "alk" and "Ar" is an independently selected alkylene or arylene, respectively;

Y is selected from the group consisting of $-H$, alkyl, alkenyl, alkynyl, aryl, alicyclic, heteroalicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted;

R^1 is independently selected from the group consisting of $-H$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$ -aryl, $-alk-aryl$, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, $-alk-S-C(O)R^3$, $-alk-S-S-alkylhydroxy$, and $-alk-S-S-S-alkylhydroxy$, or together R^1 and R^1 are $-alk-S-S-alk-$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl,

or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-\text{CH}_2 \text{OH}$, $-\text{CH}_2 \text{OCOR}^3$, $-\text{CH}_2 \text{OC(O)SR}^3$, $-\text{CH}_2 \text{OCO}_2 \text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2 \text{N}_3$, $-\text{CH}_2 \text{NR}^2_2$, $-\text{CH}_2 \text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH}(\text{CH}=\text{CR}^2 \text{R}^2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all $-\text{H}$; and
- b) when Z is $-\text{R}^2$, then at least one of V and W is not $-\text{H}$ or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and $-\text{H}$;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower alicyclic, and lower heteroalicyclic;

R^6 is independently selected from the group consisting of $-\text{H}$, and lower alkyl;

R^7 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-\text{C(O)R}^{10}$;

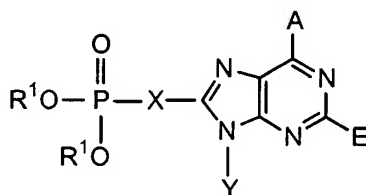
R^8 is independently selected from the group consisting of $-\text{H}$, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-\text{C(O)R}^{10}$, or together said R^8 groups form a bidendate alkylene;

R^9 is selected from the group consisting of alkyl, aralkyl, alicyclic, and heteroalicyclic;

R^{10} is selected from the group consisting of $-\text{H}$, lower alkyl, $-\text{NH}_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-OH$, $-NH_2$ and $-OR^3$; and pharmaceutically acceptable prodrugs and salts thereof.

50. (New) A pharmaceutical composition comprising a pharmaceutically effective amount of an FBPase inhibitor of formula 1:



wherein

A is selected from the group consisting of $-NR^8$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, halo, lower alkyl, $-CON(R^4)_2$, guanidino, amidino, $-H$, and perhaloalkyl;

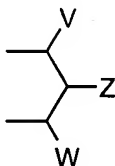
E is selected from the group consisting of $-H$, halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-CN$, and $-NR^7$;

X is selected from the group consisting of $-alk-NR-$, alkylene, alkenylene, alkynylene, arylene, heteroarylene, $-alk-NR-alk-$, $-alk-O-alk-$, $-alk-S-alk-$, $-alk-S-$, alicyclicene, heteroalicyclicene, 1,1-dihaloalkylene, $-C(O)-alk-$, $-NR-C(O)-NR'$, $-alk-NR-C(O)-$, $-alk-C(O)-NR-$, $-Ar-alk-$, and $-alk-Ar-$, all optionally substituted, wherein each R and R' is independently selected from $-H$ and lower alkyl, and wherein each "alk" and "Ar" is an independently selected alkylene or arylene, respectively;

Y is selected from the group consisting of $-H$, alkyl, alkenyl, alkynyl, aryl, alicyclic, heteroalicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2$, and $-OR^3$, all except H are optionally substituted;

R^1 is independently selected from the group consisting of $-H$, alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$ -aryl, $-alk-aryl$, $-C(R^2)_2OC(O)NR^2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2$

OC(O)SR^3 , $-\text{alk-S-C(O)R}^3$, $-\text{alk-S-S-alkylhydroxy}$, and $-\text{alk-S-S-S-alkylhydroxy}$, or together R^1 and R^1 are $-\text{alk-S-S-alk-}$ to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-\text{R}^9$; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC(O)SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2_2$, $-\text{CH}_2\text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH(CH=CR}^2\text{R}^2)\text{OH}$, $-\text{CH(C}\equiv\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

- a) V, Z, W are not all $-\text{H}$; and
- b) when Z is $-\text{R}^2$, then at least one of V and W is not $-\text{H}$ or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and $-\text{H}$;

R³ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R⁴ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R⁵ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower alicyclic, and lower heteroalicyclic;

R⁶ is independently selected from the group consisting of -H, and lower alkyl;

R⁷ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and -C(O)R¹⁰;

R⁸ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, -C(O)R¹⁰, or together said R⁸ groups form a bidendate alkylene;

R⁹ is selected from the group consisting of alkyl, aralkyl, alicyclic, and heteroalicyclic;

R¹⁰ is selected from the group consisting of -H, lower alkyl, -NH₂, lower aryl, and lower perhaloalkyl;

R¹¹ is selected from the group consisting of alkyl, aryl, -OH, -NH₂ and -OR³; and pharmaceutically acceptable prodrugs and salts thereof.

Remarks

Support for the new claims can be found throughout the specification. For instance, p. 6, lines 17-20, 23-25, p. 61, lines 15-16, p. 61, line 27 - p. 62, line 4, as well as in original claims 35-37, and 41.